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Biosketch

York's academic career has spanned nearly thirty (30) years and his research interests are cellular communication pathways with relevance to disease pathophysiology. His lab's discoveries of signaling pathways and metabolism have led to field-defining paradigms. York has been a leader in institutional missions that have helped shape strategic and long-term support for universities and industry both as Chair of the Department of Biochemistry (Vanderbilt University) and Chief Science Officer at Impossible Foods, Inc (a mission-based hyper-growth startup company seeking to reduce climate change and restore biodiversity through plant-based meat). As a leader, York has sought to foster an inclusive and enriching environment that is paramount to success in research, education and technology development. York has trained, mentored and taught hundreds of scholars including: faculty, post-doctoral fellows, graduate students, undergraduates and high-school students.

Key Publications

"A phospholipase C-dependent inositol polyphosphate kinase pathway required for efficient mRNA export" (1999) *Science*, 285, 96-100. PMID: 10390371

"A role for nuclear inositol 1,4,5-trisphosphate kinase in transcriptional control" (2000) *Science*, 287, 2026-2029. PMID: 10720331

"A conserved family of enzymes that phosphorylate inositol hexakisphosphate" (2007) *Science* 316, 106-109. PMID: 17412958

"Understanding Cellular Signaling Networks"

Nucleotidases and Phosphatases - Since we discovered the structurally conserved family of lithium-inhibited phosphatases (York JD et al PNAS 1995) we have identified seven gene products as members. We have discovered a role for sulfur assimilation in the pathophysiology of chondrodysplasia (Frederick et al PNAS 2008), anasarca (Hudson et al PNAS 2013), iron deficiency anemia (Hale AT et al PNAS 2018), and lithium mechanism of action (Eisele BS et al JBC 2021; Dollins DE et al JBC 2021)

Inositol Phosphate Kinases: Our studies of cellular signaling have defined the synthesis and cellular functions of inositol hexakisphosphate (IP6) (York et al Science 1999). Critical insights into the biology of IP6 as a regulator of mRNA export and a structural cofactor are ongoing. Additionally, we identified an IP3 kinase is a transcriptional activator (Odom A et al Science 2000). Importantly, we identified these genes are conserved from yeast to man and their IPx products are required for proper organismal development in flies, plants and mice (Frederick et al PNAS 2005; Stevenson-Paulik et al PNAS 2005; Seeds et al PNAS 2015). Ongoing work seeks to define the receptors and mechanisms of action of IP6 chemical.

Inositol Diphosphate Metabolism and Signaling: We have defined metabolic and functional pathways of inositol pyrophosphates (high-energy diphosphoryl inositol phosphate molecules - IP7 and IP8). These include: in the regulation of telomere length (York, S. et al JBC 2005) cloning and characterization of novel kinase, Vip1 (Mulugu S et al Science 2007) and collaborative studies with Erin O'Shea lab (Lee YS et al Science 2007). We determined the structure of the Vip1 product as 1-IP7 by NMR (Lin et al, JBC 2009) and X-ray crystallography (Dollins, DE et al PNAS 2020). We also deteremined VIP1 dual-functional kinase/pyrophosphatase switch (Mulugu S et al Science 2007; Fridy et al JBC 2009; Dollins DE et al PNAS 2020).